REMARKS

Claims 3-8, 10, 43, 44 and 56-59 are cancelled herein without prejudice or disclaimer and Applicant reserves the right to claim subject matter of the cancelled claims in one or more continuing patent applications. Claims 1 and 42 are amended herein and claims 60-71 are new. Basis for the amendments and the newly claimed subject matter is in the claims as originally filed and in the specification throughout. Representative basis for chromosome positions is in paragraphs 0224, 0234 and 040 of the specification, for example. The chromosome position in claims 65 and 71 is extrapolated from position 18828 in SEQ ID NO: 1 using information in Table 9 of paragraph 0224. Accordingly, entry of the claim amendments and new claims will not introduce any prohibited new matter.

The Office rejected claims in the outstanding action for alleged lack of written description, alleged lack of enablement and alleged anticipation, which are summarized hereafter:

i. Claims 1-4, 7-10, 42-45 and 56-59 were rejected under 35 U.S.C. 112, first paragraph, for the specification allegedly lacking a written description;
ii. Claims 1-4, 7-10, 42-45 and 56-59 were rejected under 35 U.S.C. 112, first paragraph, for the specification allegedly lacking an enabling disclosure; and
iii. Claims 56, 58 and 60 were rejected under 35 U.S.C. 102(b) for alleged anticipation by Severin.

Claim rejections in the outstanding Office action are traversed, and are moot in view of the amendments herein. Applicant does not necessarily accept or agree with rejections set forth in the Office action, and the claim amendments, claim cancellations and new claims are submitted herein for the purpose of expediting prosecution. Remarks in response to the outstanding claim rejections are set forth hereafter.

Rejection for Alleged Lack of Written Description

The Office rejected claims 1-4, 7-10, 42-45 and 56-59 for the specification allegedly lacking a written description of the claimed subject matter. Applicant respectfully notes the rejection is inapplicable to claims 3-8, 10, 43 and 56-59 as they are

cancelled herein without prejudice or disclaimer, and the rejection is inapplicable to amended claims 1 and 42 and the remaining claims. The rejection is traversed in view of the reasoning presented hereafter.

Well-accepted principles of genetics support a finding that Applicant's specification provides a written description of the claimed subject matter. The concept of linkage disequilibrium in genetics embodies the phenomenon that a disease-associated region in the human genome contains a cluster of polymorphisms associated with a disease state. Specifically,

> markers very close to the disease gene will tend, more likely than average, to retain the haplotype of the original chromosome because, as the distance to the disease gene shrinks, it becomes less likely that recombination events will have occurred in this particular region.

From Cantor & Smith, *Genomics: The Science and Technology Behind the Human Genome Project*, 1999, John Wiley & Sons, Inc., New York, page 192. Thus, identifying multiple polymorphisms associated with a disease state also identifies a region associated with the disease state consistent with the concept of linkage disequilibrium.

The specification analyzed several polymorphisms in the region of the human genome that includes the sub-region specified by claims 1 and 42. This claimed sub-region is between about chromosome position 117925391 and about chromosome position 117945870. Applicant identified polymorphic variants in this region as being in linkage disequilibrium and particularly associated with breast cancer (e.g., specification, paragraph 013, and Figure 4). Thus, Applicant clearly identified the claimed sub-region as associated with breast cancer, and therefore had possession of the claimed subject matter.

The claimed sub-region is within a larger region between about chromosome position 117912256 and about chromosome position 117995524 according to Build 31 of the GenBank database, and Applicant identified several polymorphic variants in this larger region associated with breast cancer. For example, please see Tables 12 and 17

on pages 70 and 76 of the specification, which identified six (6) polymorphisms associated with breast cancer with a p-value of less than 0.05 of the sixty (60) polymorphisms analyzed in the claimed region. Thus, the specification provided a written description for the claimed subject matter in the specification because Applicant disclosed several polymorphisms associated with breast cancer in the claimed region, and thereby identified the region as being associated with breast cancer in accordance with principles of genetics.

Further, Applicant analyzed a representative number of polymorphisms in the region spanning chromosome position 117912256 to position 117995524 in the process of identifying a subset of polymorphisms associated with breast cancer. Applicant has determined from a current search of the HapMap database (July 2006 release) that 182 single nucleotide polymorphisms have been genotyped in the region designated by claim 1. In the subject specification, Applicant analyzed 60 single nucleotide polymorphisms in this region before the filing date of November 25, 2003. For example, Table 12 on page 70 of the specification analyzed 58 of the polymorphisms and Table 17 on page 76 of the specification analyzed two newly-identified polymorphisms. Further, of the 182 polymorphisms in the HapMap database in this region, only 78 have a frequency of 0.05 or more. Of the 60 polymorphisms analyzed in Applicant's specification, however, 43 have a frequency of 0.05 or more. Thus, Applicant (i) analyzed about one-third (33%) of the number of single nucleotide polymorphisms in the region reported in the HapMap database, (ii) analyzed over half (55%) of the number of single nucleotide polymorphisms in the region reported in the HapMap database having a frequency of 0.05 or more, and (iii) identified a subset of polymorphisms associated with breast cancer. The specification therefore provides a written description for the claimed subject matter as Applicant analyzed a representative number of polymorphisms in the region of human DNA that includes the claimed region.

Applicant also provided biological evidence that associated the analyzed region with breast cancer. For example, Applicant compared levels of mRNA encoded by the analyzed genomic region and found target mRNA levels were lower in normal, immortalized breast cell lines, while higher levels were identified in tumorigenic breast

cancer cell lines (e.g., specification, paragraph 0239). Also, inhibiting the target region by specific siRNA molecules significantly reduced proliferation of breast cancer cells (e.g., specification, paragraphs 0242 and 0243). Applicant also demonstrated that breast cancer cell lines in which the target region was inhibited by specific siRNA molecules were significantly more sensitive to chemotherapeutic agents that cell lines not treated with the siRNA molecules (e.g., specification, paragraph 0247). This latter study provides additional evidence that the target region is associated with breast cancer. Thus, Applicant demonstrated by biological data that the target region was significantly associated with breast cancer.

Accordingly, the specification provides a written description of the claimed subject matter consistent with 35 U.S.C. 112, first paragraph, demonstrating that Applicant had clear possession of the claimed subject matter. Applicant therefore respectfully requests withdrawal of the rejection.

Rejection for Alleged Lack of Enablement

The Office rejected claims 1-4, 7-10, 42-45 and 56-59 for the specification allegedly lacking an enabling disclosure of the claimed subject matter. Applicant respectfully notes the rejection is inapplicable to claims 3-8, 10, 43, 44 and 56-59 as they are cancelled herein without prejudice or disclaimer, and the rejection is inapplicable to amended claims 1 and 42 and the remaining claims. The rejection is traversed in view of the reasoning presented hereafter.

Applicant's specification identifies a region specified in claims 1 and 42 associated with occurrence of breast cancer. Given the discussion regarding genetics principles above, Applicant's finding paves the way towards identifying and using polymorphisms of this region in the claimed methods. Applicant's finding that the region specified in claims 1 and 42 is associated with breast cancer is useful for guiding the person of ordinary skill in the art towards routinely identify any other polymorphisms associated with breast cancer in that region. The routine nature of any experimentation extending beyond the results described in Applicant's specification is underscored by the clear teachings and guidance in the specification, as elucidated hereafter.

The specification provides multiple working examples in support of the claimed subject matter, an *Ex Parte Foreman* factor bearing on enablement addressed in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). For example,

(i) paragraphs 0215 to 0223 describe methodology for identifying polymorphisms associated with breast cancer in DNA from a human subject;

(ii) paragraphs 0224 to 0229 describe methods and components for identifying polymorphisms associated with breast cancer in DNA from a subject in the region specified by claims 1 and 42;

(iii) paragraphs 0230 to 0234 describe deep sequencing and genotype analysis of polymorphisms associated with breast cancer; and

(iv) paragraphs 0208 to 0209 describe methods for isolating DNA from human blood samples.

In addition to this set of working examples for performing the claimed methods, the specification also provides clear guidance to the person of ordinary skill in the art for the scope of the claimed subject matter, another factor addressed in *In re Wands* (supra). For example, the specification in paragraphs 0100 to 0104 provides clear guidance for performing multiple types of assays useful for identifying polymorphisms associated with breast cancer.

The Court of Appeals for the Federal Circuit (CAFC) has found some experimentation is acceptable to produce an invention, and routine experimentation does not preclude a finding of enablement (*Monsanto Co. v. Scruggs*, 459 F.3d 1328; 79 USPQ.2d 1813 (Fed. Cir. 2006) and *In re Wands* (supra)). Given that the working examples and clear guidance in the specification teach multiple methods for identifying polymorphisms associated with breast cancer, the person of ordinary skill in the art could apply these methods in a routine manner to polymorphisms in the region specified by claims 1 and 42 and perform the claimed methods.

The facts and reasoning on which the CAFC found enablement in *In re Wands* are applicable to the same finding of enablement here. In the *Wands* case, the Office erred in rejecting the Applicant's claim to immunoassay methods using a specified generic class of antibodies. The Applicant made a public deposit of a hybridoma cell line that

secreted only a specific antibody, yet the CAFC found those skilled in the monoclonal antibody art could, using the state of the art and Applicant's written disclosure, produce and screen other hybridomas secreting other monoclonal antibodies falling within the generic class without undue experimentation.

The technology in *Wands* is similar to the technology described in the present specification in the sense that the person of ordinary skill in the art is prepared to screen additional polymorphisms in the region specified by claims 1 and 42. The specification has disclosed a region of the human genome associated with breast cancer, and the person of ordinary skill in the art now (i) is guided to that region, and (ii) motivated to routinely identify any other polymorphisms in the region associated with breast cancer, should they exist. Further, multiple screening methods are well-known in the art, as described above, and suited to automated screening platforms. Thus, the rationale in *In re Wands* is applicable to a finding of enablement here.

These factors, coupled with the high level of skill in the art for technology pertaining to the pending claims, leads to the conclusion that any experimentation associated with the full claim scope is routine and not undue. Accordingly, the specification provides an enabling disclosure of the claimed subject matter consistent with 35 U.S.C. 112, first paragraph. Applicant therefore respectfully requests withdrawal of the rejection.

Rejection for Alleged Anticipation

The Office rejected claims 56, 58 and 60 under 35 U.S.C. 102(b) for alleged anticipation by Severin. Applicant respectfully requests clarification of the rejection as there was no claim 60 pending as of the time the Office issued the action. The rejection, however, is moot given the cancellation of claims 56-59, and withdrawal of the rejection respectfully is requested.

CONCLUSIONS

Applicant respectfully submits all pending claims will be in condition for allowance upon entry of the amendments herein. Applicant respectfully solicits a prompt notification to this effect, and the Examiner is encouraged to contact the undersigned representative (contact information below) to promptly resolve any remaining issues or questions.

In the unlikely event a relevant document is separated from this Amendment and the Office determines that an extension and/or other relief is required, Applicant petitions for any required relief, including extensions of time, and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 50-3473**.

Respectfully submitted,

Dated: May 18, 2007

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